USSN 09/975,350
Art Unit: 1618

REMARKS

Status of Claims

Current Status

Claims 1, 3, 4, 8-50, 55-61 and 63-68 are pending. Claims 36-44, 57, 58, 60, 61, 64 and 65 are withdrawn from consideration. Claims 1, 3, 4, 8-35, 45-50, 55, 56, 59, 63 and 66-68 are rejected.

Present Reply

In this reply claims 41 and 42 are amended, and claims 44 and 61 are canceled. Upon entry of the present amendment, claims 1, 3, 4, 8-43, 45-50, 55-60 and 63-68 will be pending in this application, with claims 36-43, 57, 58, 60, 64 and 65 being withdrawn from consideration. No new matter has been added by way of these amendments.

Claim Rejections

Reconsideration and allowance of all claims is hereby respectfully requested in light of the following discussion.

Rejection under 35 U.S.C. §102

Claims 1, 3, 4, 11, 14, 15, 32, 33, 45-47, and 59 are rejected under 35 U.S.C. §102(b) as being anticipated by Nguyen et al. (US 5,843,347). The Examiner alleges that the lyophilized composition of Nguyen is a "solid solution." Applicants have carefully considered the Examiner's position, but respectfully disagree that the lyophilized composition of Nguyen is a solid solution.

The Nguyen reference teaches that the lyophilization process preserves the initial characteristics of the active ingredient as it existed in the pre-lyophilized composition (*see* col. 2, lines 46-50 and 53-56; col. 3, lines 11-12 and 17-22). In other words, if the active ingredient was present as discrete undissolved particles prior to lyophilization, then the active ingredient continues to be present as discrete undissolved particles in the lyophilized product.

Applying this teaching to the lyophilized compositions of Nguyen in Examples 16 and 17, Nguyen indicates that if the modafinil active ingredient is present as discrete undissolved particles in the pre-lyophilized compositions (i.e., the "pasty mixtures"), then it is also present as discrete undissolved particles in the lyophilized products (lyophilizates). The pre-lyophilized

compositions of Examples 16 and 17 contain (a) modafinil (100 g) as the active ingredient, (b) various solid ingredients (55 g -115 g total), and (c) water (200 g). Because modafinil is insoluble in water (solubility = 0.4 g/L), it is necessarily true that the pre-lyophilized compositions of Nguyen contain significant quantities of discrete undissolved particles of modafinil (col. 7, lines 25-27; col. 8, lines 23-24). Because the undissolved modafinil particles do not dissolve and form a solution during the lyophilization process (see above), it is necessarily true that the finished lyophilized products of Nguyen also contain significant quantities of discrete undissolved modafinil particles.

Compositions that contain significant quantities of undissolved particles are fundamentally different from the compositions of the present invention because such compositions are not solid solutions. In a solid solution, each component is completely dissolved in the mixture – i.e., the components are homogeneously mixed at the molecular level (*see* (a) U.S. Patent No. 6,264,981 at col. 6 lines 35-39, col. 6 line 67 to col. 7 line 4, col. 8 lines 45-47, and col. 8 lines 65-67; (b) U.S. Patent No. 5,422,384 at col. 2, lines 45-52; *and* (c) Sertsou, G. et al., "Factors affecting incorporation of drug into solid solution with HPMCP during solvent change co-precipitation," *Int. J. Pharmaceutics*, **2002**, *245*, 99-108 at 100, first full paragraph of first column). Solid solutions – like liquid solutions – are fundamentally different from the suspensions and emulsions disclosed in Nguyen because solid solutions do not contain discernible phase boundaries and do not contain discrete undissolved particles.

Because the lyophilized products of Nguyen contain significant quantities of discrete undissolved modafinil particles, the Nguyen compositions are not solid solutions. In view of the fact that Nguyen fails to disclose a solid solution, Nguyen fails to disclose each limitation of the pending claims and Nguyen is not an anticipatory reference. Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. §103

Nguyen:

Claims 8-10, 12, 13, 16-31, 34, 35, 55, 56, 63, 66 and 68 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nguyen et al. (US 5,843,347). The Examiner alleges that the lyophilized composition of Nguyen is a "solid solution." Applicants have carefully considered

the Examiner's position, but respectfully disagree that the lyophilized composition of Nguyen is a solid solution.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate that a prior art reference teaches or suggests all of the limitations of the rejected claims (MPEP § 2142). As discussed above, the compositions of Nguyen contain undissolved modafinil particles. There is no motivation to modify the undissolved particle compositions of Nguyen to form solutions because Nguyen teaches that its lyophilized microbead products are suitably prepared from suspensions or emulsions containing undissolved particles (col. 7, lines 2-28; col. 8, lines 23-24). And even if a person of ordinary skill was motivated to prepare a modafinil solution, Nguyen provides no direction on how to prepare such a mixture, given that modafinil is insoluble in water (solubility = 0.4 g/L).

In view of the fact that Nguyen fails to teach or suggest a solid solution of modafinil, Nguyen does not teach or suggest each limitation of the rejected claims and therefore cannot render the rejected claims obvious. Applicants respectfully request that this rejection be withdrawn.

Nguyen and Grebow:

Claims 47-50, 55, 56, 67 and 68 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Grebow (US 5,618,845). The Examiner alleges that the lyophilized composition of Nguyen is a "solid solution." Applicants have carefully considered the Examiner's position, but respectfully disagree that the lyophilized composition of Nguyen is a solid solution.

As discussed above, Nguyen does not teach or suggest a solid solution. Grebow fails to cure the deficiencies of Nguyen. The Grebow reference is concerned with discrete solid particles, not solutions. Specifically, the Grebow reference is directed to a pharmaceutical composition comprising discrete modafinil particles having a defined particle size (col. 2, lines 6-8). The Grebow invention is based on the discovery that the size of a solid modafinil particle is important to the potency and safety of the drug (col. 2, lines 8-10). According to the Grebow disclosure, the preferred mean particle size of a solid modafinil particle is from about 2 microns to about 19 microns (col. 2, lines 51-53), the preferred median particle size of a solid modafinil particle is from about 2-60 microns (col. 2, lines 56-58), and the preferred mode particle size of a

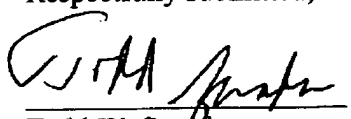
solid modafinil particle is from about 2-60 microns (col. 2, lines 61-63). Grebow states that the solid modafinil particles having a defined particle size can be present in a pharmaceutical composition, which may be a tablet, capsule, powder, pill, liquid/suspension or emulsion (col. 4, lines 12-18 & col. 10, lines 18-21). Importantly, each of these pharmaceutical compositions contains solid modafinil particles of a defined particle size. There is no motivation to modify the Grebow disclosure to form a modafinil solution because such a modification would dissolve and thus destroy the solid modafinil particles of defined particle size, which form the basis of the Grebow invention (col. 4, lines 53-55). Modifying Grebow to dissolve the solid modafinil particles of defined particle size would require a fundamental departure from the teaching of the reference. Accordingly, Grebow does not teach or suggest a solid solution.

In view of the fact that Nguyen and Grebow fail to teach or suggest a solid solution, Nguyen and Grebow do not teach or suggest each limitation of the rejected claims and therefore cannot render the rejected claims obvious. Applicants respectfully request that this rejection be withdrawn.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. It is believed that all the claims are in form for allowance, and an early notification to that end is respectfully requested. Applicants invite the Examiner to contact the undersigned at (610) 883-5679 to clarify any remaining issues.

Respectfully submitted,



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